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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte **The University of Pennsylvania,**
Inventors: William F. Degrado, Dahui Liu, Gregory N. Tew,
Michael L. Klein, Jing Yuan, and Sungwook Choi

Appeal 2010-005832
Application 10/801,951
Technology Center 1600

Before JAMES T. MOORE, *Vice Chief Administrative Patent Judge*, and RICHARD E. SCHAFER and HUBERT C. LORIN, *Administrative Patent Judges*.

SCHAFER, *Administrative Patent Judge*.

DECISION ON APPEAL

The University of Pennsylvania (Applicant) appeals the Examiner's decision rejecting Claims 16-48 and 67-73 on the ground of obviousness-type double patenting. Because we do not see reversible error in the Examiner's conclusion that administering an effective amount of certain compounds to treat microbial infections would have been obvious from the method of using many of those same compounds for killing microorganisms on a surface, we affirm.

The Claimed Subject Matter

Applicant's invention is directed to a method of treating animals having a microbe caused infection. The method has a single step -- administering an effective amount of a composition including at least one of a very large class of specified oligomers in a pharmaceutically acceptable carrier or diluent. Administering may be topical or systemic to any body site or tissue. Written Description, ¶ 0063. The oligomers are identified by the following Formula II:

$$R^1\text{-}[x\text{-}A_1\text{-}x\text{-}y\text{-}A_2\text{-}y\text{-}]_m\text{-}R^2 \qquad \text{II}$$

Each of R^1, R^2 x, y, A_1, and A_2, are defined using the Markush format. Additionally, the oligomer must be amphiphilic. Amphiphilic compounds include hydrophilic (water attracting) and lipophilic (fat attracting) portions. Independent Claim 16 is representative and reproduced below with the Markush definitions excluded:

> A method of treating a microbial infection in an animal in need thereof, said method comprising
>
> administering to the animal an effective amount of a pharmaceutical composition comprising an amphiphilic oligomer of Formula II:
>
> $$R^1\text{-}[x\text{-}A_1\text{-}x\text{-}y\text{-}A_2\text{-}y\text{-}]_m\text{-}R^2 \text{ (II)}$$
>
> or an acceptable salt or solvate thereof, wherein:

> [R^1, x, A_1, x, y, A_2, y and R^2 are specifically defined],
> m is 1 to about 20; and a pharmaceutically acceptable carrier or diluent.

Brief, 27 (Claims Appendix). A complete copy of Claim 16 is reproduced in the Appendix attached to this opinion.

The Rejection

The Examiner rejected the subject matter of Claims 16-48 and 67-73 on the basis of obviousness-type double patenting of Claims 1, 4-8, 11, 14-15, 20-22, and 26 of DeGrado.[1] DeGrado's claims are directed to a method of killing microorganisms requiring two steps: (1) providing a substrate having on its surface certain specified "contact killing" facially amphiphilic polymers or oligomers and (2) contacting that substrate with a microorganism. For the purpose of deciding this appeal DeGrado's Claim 26 is the most relevant and reproduced below:

> 26. A method of killing microorganisms, said method comprising the steps of:
> Providing a substrate having disposed thereon a contact killing, facially amphiphilic polymer or oligomer of claim 1, claim 14, or claim 20;
> Placing said facially amphiphilic polymer or oligomer disposed thereon on said substrate in contact with a microorganism to allow formation of pores in the cell wall of said microorganism.

Claims 1, 14, and 20, from which Claim 26 depends, identify a very large class of polymers and oligomers useful in the process. DeGrado's Claims 1,

[1] U.S. Patent 7,173,102.

14, and 20 define the polymers and oligomers in terms of Formulas I, II, and IV, respectively. DeGrado's Formula II from Claim 14 is reproduced below:

$$R^1\text{-}[x\text{-}A\text{-}x\text{-}y\text{-}B\text{-}y\text{-}]_m\text{-}R^2 \text{ (DeGrado II).}$$

The empirical formula is identical to Applicant's Formula II in rejected Claim 16 with "A" substituted for Applicant's A_1 moiety and "B" substituted for Applicant's A_2 moiety. Each of the DeGrado moieties is defined in the Markush style. The subscript "m" in DeGrado's Claim 26 is defined as "2 to at least about 500."

The Examiner held that Applicant's claims were not patentably distinct from DeGrado's claims. Answer, 3. The Examiner determined that the person of ordinary skill in the art would have understood "substrate" as used in DeGrado's claims to encompass any surface including skin or internal organs of an animal having a microbial infection. Answer, 4. The Examiner determined that in light of DeGrado's general teaching that the compounds inhibit microorganisms when applied to a substrate, the person of ordinary skill would have been motivated to administer the DeGrado compositions in a pharmaceutical composition to an infected animal with a reasonable expectation of success. Answer, 4-5.

Analysis

Claim 16

Applicant's Claim 16 is directed to a method for treating microbial infections in mammals by "administering" a composition containing certain amphiphilic compounds of Formula II in a carrier. "Administering" includes topical application to "any body site or tissue." Written Description, ¶ 0063. DeGrado's Claim 26 is directed to a method for killing microorganisms by contacting the microorganisms with a substrate including the facially

amphiphilic compounds described in DeGrado's Claims 1, 14, and 20. Those claims, like the claims under rejection, encompass an extraordinarily large number of compounds. Applicant has not contended that the compounds defined in its Claim 16 do not encompass a large number of the facially amphiphilic compounds described in DeGrado's Claim 26.

DeGrado's Claim 26 describes a process for killing microorganisms by contacting the microorganisms with a substrate having a "contact killing" amphiphilic polymer on the surface. The contact-killing polymers are defined by DeGrado's Claims 1, 14, and 20, and incorporated by reference into Claim 26. DeGrado's Claim 26 is an assertion by DeGrado that all of the large numbers of the compounds which are encompassed by that claim are operative to achieve the contact-killing utility. *See, In re Marzocchi*, 439 F.2d 220, 223 (CCPA 1971) ("Accepting, therefore, that the term is a generic one, its recitation must be taken as an assertion by appellants that all of the 'considerable number of compounds' which are included within the generic term would, as a class, be operative to produce the asserted [utility].") Presumably, DeGrado had a reasoned basis for believing that each of the large number of compounds encompassed by DeGrado's Claim 26 possessed that contact-killing utility. Applicant has not argued that a person having ordinary skill in the art would have a basis to doubt the contact-killing utility of any of the compounds encompassed by DeGrado's Claim 26. Additionally, the PTO does not have the resources to perform tests to verify whether any or all of the DeGrado compounds are antimicrobial. Accordingly, the PTO must, in the absence of a reason to the contrary, accept the truthfulness of DeGrado's assertions. On the record

before us we see no reason to doubt DeGrado's assertion of the contact-killing utility of all the compounds encompassed by DeGrado's Claim 26.

Because compounds of DeGrado's Claim 26 are taught to kill microorganisms on contact when incorporated in or on a substrate, one having ordinary skill in the art would have recognized and appreciated that the compounds of DeGrado's Claim 26 would be useful for killing microorganisms on contact when incorporated in a carrier or diluent to form a topical antimicrobial composition. It would, therefore, have been prima facie obvious to administer a composition including an effective amount of the compounds of DeGrado's Claim 26 in a carrier as a topical antimicrobial composition for administration to the infected skin of an animal.

Applicant argues that the Examiner has misconstrued the word "substrate" in DeGrado's Claim 26 as encompassing any surface in need of killing a microorganism including skin or internal organs of an animal. Brief, pp. 15-17. In Applicant's view, the DeGrado

> patent disclosure, taken as a whole, indicates the term "substrate" was intended to encompass inanimate surfaces, *not* living tissues.

Brief, 16 (emphasis in original). Applicant directs us to various portions of DeGrado's disclosure said to show that the substrate is limited to non-living surfaces. DeGrado's disclosure, however, says: "Any object that is exposed to or susceptible to bacterial or microbial contamination can be treated with these polymers." DeGrado, 27: 5-6; 29: 61-62. While DeGrado's disclosure only exemplifies inanimate surfaces, the patent also states:

> The facially amphiphilic polymer may be attached to, applied on or incorporated into <u>almost any substrate</u> including <u>but not limited to</u> woods, paper, synthetic

> polymers (plastics), natural and synthetic fibers, natural and synthetic rubbers, cloth, glasses and ceramics by appropriate methods including covalent bonding, ionic interaction, coulombic interaction, hydrogen bonding or cross-linking.

DeGrado, 26: 47-54 (emphasis added). Considering the above-quoted portions of DeGrado's disclosure, as well as the disclosure as a whole, we construe "substrate" as used in DeGrado's Claim 26 as not limited to inanimate surfaces. We construe the word as also encompassing living substrates such as skin. In this regard we note, that neither of the two declarants relied upon by Applicant, testify that one skilled in the art would understand "substrate" as used in the DeGrado's specification to be limited to non-living substrates.

In any event, even if the Examiner erred in construing "substrate," that error was harmless. In holding that one of ordinary skill in the art would be motivated to administer the compounds to an animal, the Examiner also relied on the "general teaching that the [DeGrado] oligomers inhibit the growth of microorganisms on a surface." Answer, 4. As we noted above, DeGrado's Claim 26 teaches that the compounds kill microorganisms on contact. It would have been prima facie obvious to administer those compounds as part of a topical antimicrobial composition including a conventional carrier or diluent to kill microorganisms at the site of a skin infection.

Applicant relies on the Declarations of Drs. David P. Nicolau and Harry Bermudez in arguing that the person of ordinary skill would not have expected the compounds to be effective for treating a microbial infection when administered to an animal. Brief, 17-18. Applicant specifically

directs us to Dr. Nicolau's testimony, appearing at Paragraph 8 of his Declaration, that

> a person of ordinary skill in the art would not necessarily expect a polymer shown to function as an antimicrobial agent when attached to or incorporated into an object to be effective in treating a microbial infection in an animal.

Brief 17 (emphasis added). Dr. Bermudez similarly testifies

> that a person of ordinary skill in the art would not expect that a polymer to be applied to the surface of, or incorporated into, an object would necessarily be effective when administered to an animal to treat a microbial infection.

Bermudez Declaration, p. 3, ¶ 7 (emphasis added).

Obviousness only requires that the person of ordinary skill in the art have a reasonable expectation that the beneficial result will be achieved. *See In re Merck & Co., Inc.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986). DeGrado's Claim 26 teaches that the compounds defined therein kill microorganisms on contact when incorporated into or on a substrate. This teaching alone is sufficient to give rise to a reasonable expectation that the compounds will kill microorganisms that are contacted when the compounds are topically administered with a conventional diluent or carrier. Neither Dr. Bermudez nor Dr. Nicolau have provided any explanation or factual basis for concluding that that compounds taught to kill microorganisms on contact when on or incorporated in a substrate would not be expected to kill those same microorganisms when incorporated in a carrier or diluent for topical application to an infection.

Relying on Dr. Bermudez's Declaration, Applicant argues that one skilled in the art would not conclude from the DeGrado patent the polymers are not toxic and would be safely administered as part of a pharmaceutical composition. Brief, 18.

Under the facts of this appeal, we fail to see the relevance of this argument to the obviousness determination. The knowledge that a microbe-killing compound is non-toxic is not a necessary requirement in judging the obviousness of the use of that compound to treat infections. While evidence that the prior art compounds were toxic to animals might be relevant as teaching away from using the compounds as an antimicrobial, we have not been directed to any such evidence. Neither Dr. Bermudez or Dr. Nicolau testify that those working in the art would have viewed the DeGrado compounds as toxic. Indeed, the only evidence to which we have been directed, relating to the toxicity of the DeGrado compounds appears in DeGrado's Specification. That Specification does not indicate any toxicity concerns. To the contrary, DeGrado says: "The polymeric materials are further designed to have low toxicity to mammalian cells." DeGrado, 5:15-17.

Applicant also argues that the range of values for "m" in Formula II of the rejected claims patentably distinguishes those claims from DeGrado's Claim 26. Brief, 19-22. "m" in the rejected claims refers to the number of repeating polymeric units and is specified as 1-20 in some of Applicant's claims, 1-10 in others and as 1-3 in still others. In DeGrado's Claim 26, "m" is specified as 2-500. Because of DeGrado's broad range, the Examiner is said not to have established that the compounds of the rejected claims are

prima facie obvious over the compounds of the claims of the DeGrado patent. Brief, 19.

DeGrado's Claim 26 specifies "m" as 2 to about 500. The values of "2" and "500" are expressly described and incontrovertibly part of the presumed "prior art" for the purpose of obviousness-type double patenting. The former value is within the specified value of "m" in each of Applicant's rejected claims. The express description that "m" is 2 is sufficient to establish prima facie obviousness for at least that specific value. To the extent that other claimed values for "m" would not have been obvious from either the described value of "2" or from the range of 2 to about 500, the claims are still unpatentable. Claims which read on patentable, as well as unpatentable subject matter, are considered unpatentable. *In re Freeman*, 474 F.2d 1318, 1323 (CCPA 1973); *In re Landgraf*, 436 F.2d 1046, 1049-50 (CCPA 1971); *In re Muchmore*, 433 F.2d 824, 826 (CCPA 1970).

Additionally, the evidence to which we have been directed is insufficient to establish a reason to doubt DeGrado's representation that the compounds disclosed by DeGrado's Claim 26 having values of m ranging from 2 to about 500 kill microorganisms on contact.

Applicant argues that one skilled in the art would have been lead away from using compounds where "m" has a value in the range of the rejected claims. Specifically, Applicant argues that DeGrado teaches that molecular weights in the range of 0.8 kD to 20 kD will be more prone to leach from the substrate. Applicant relies on Dr. Bermudez's testimony to the effect that based upon DeGrado's disclosure, one skilled in the art would have been motivated to use compounds near the higher end of the disclosed 2 – 500 range. Dr. Bermudez testifies that in his opinion, one skilled in the art

would not have expected that compounds in the range of 1 to 20 polymer units "would necessarily be effective" when administered to treat a microbial infection. Bermudez Declaration, ¶ 8.

We do not find this argument convincing. DeGrado's Claims 2-5, 9-10, 12-13, 17-18, and 23-25 appear to be to the contrary. These claims limit "m" to 2-30 indicating that compounds having" m" in that range would kill on contact notwithstanding the fact that those compounds might be prone to leach from a substrate. Additionally, Dr. Bermudez does not explain why the person of ordinary skill in the art would not believe the express teachings of DeGrado's claims, that the compounds in which "m" is in the range from 2 to 500 would kill on contact.

We affirm the rejection of Claim 16 on the basis of obviousness-type double patenting. We have considered Applicant's remaining arguments and find none that warrant reversal of the Examiner's rejections. *Cf. Hartman v. Nicholson*, 483 F.3d 1311, 1315 (Fed. Cir. 2007).

Claims 17-48 and 67-73

Applicant's Brief does not present separate arguments with respect to Claims 17-48 and 67-73. As a consequence, the dependent claims on appeal will stand or fall together. We choose Claim 16 as representative of the subject matter of those claims and affirm the Examiner's decision to reject Claims 17-48 and 67-73. 37 C.F.R. § 41.37(c)(1)(vii).

DECISION

The decision of the Examiner rejecting Claims 16-48 and 67-73 is affirmed.[2]

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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cc:

[2] Because we have affirmed the Examiner's double patenting rejection, it was unnecessary to reach and we have not considered the matters addressed in the briefing under 37 CFR § 41.50(d).

APPENDIX

Claim 16

16. A method of treating a microbial infection in an animal in need thereof, said method comprising administering to the animal an effective amount of a pharmaceutical composition comprising an amphiphilic oligomer of Formula II:

$$R^1\text{-}[x\text{-}A_1\text{-}x\text{-}y\text{-}A_2\text{-}y\text{-}]_m\text{-}R^2 \quad (II)$$

or an acceptable salt or solvate thereof, wherein:

x is NR^8, $N(R^8)N(R^8)$-, or $-C(R^7R^{7'})NR^8$, and y is C=O;
wherein R^8 is hydrogen or alkyl; R^7 and $R^{7'}$ are independently hydrogen or alkyl, or R^7 and $R^{7'}$ together are $-(CH^2)_p$-, wherein p is 4 to 8;

A_1 and A_2 are independently optionally substituted o-, m-, or p-phenylene or one of A_1 and A_2 is optionally substituted o-, m-, or p-phenylene and the other of A_1 and A_2 is optionally substituted heteroarylene, wherein A_1 and A_2 are independently optionally substituted with one or more polar (PL) groups, one or more non-polar (NPL) groups, or a combination of one or more polar (PL) groups and one or more non-polar (NPL) groups;

R^1 is

(i) hydrogen, a polar group (PL), or a non-polar group (NPL), and R^2 is $-x\text{-}A_1\text{-}x\text{-}R^1$, wherein A_1 is as defined above and is optionally substituted with one or more polar (PL) groups, one or more non-polar (NPL) groups, or a combination of one or more polar (PL) groups and one or more non-polar (NPL) groups; or

(ii) hydrogen, a polar group (PL), or a non-polar group (NPL), and R^2 is $-x\text{-}A'\text{-}x\text{-}R^1$, wherein A' is arylene or heteroarylene and is optionally substituted with one or more polar (PL) groups, one or more non-polar (NPL) groups, or a combination of one or more polar (PL) groups and one or more non-polar (NPL) groups;

(iii) $-y\text{-}A_2\text{-}y\text{-}R^2$, and R^2 is hydrogen, a polar group (PL), or a non-polar group (NPL); or

(iv) -y-A' and R^2 is -x-A', wherein A' is aryl or heteroaryl and is optionally substituted with one or more polar (PL) groups, one or more non-polar (NPL) groups, or a combination of one or

more polar (PL) groups and one or more non-polar (NPL) groups; or

(v) R^1 and R^2 are independently a polar group (PL) or a non-polar group (NPL); or

(vi) R_1 and R_2 together form a single bond;

NPL is a nonpolar group independently selected from the group consisting of $-B(OR^4)_2$ and $-(NR^{3'})_{q1NPL}-U^{NPL}-(CH_2)_{pNPL}-(NR^{3''})_{q2NPL}-R^{4'}$, wherein:

R^3, $R^{3'}$, and $R^{3''}$ are independently selected from the group consisting of hydrogen, alkyl, and alkoxy;

R^4 and $R^{4'}$ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and heteroaryl, any of which is optionally substituted with one or more alkyl or halo groups;

U^{NPL} is absent or selected from the group consisting of O, S, S(=O), $S(=O)_2$, NR^3, -C(=O)-, -C(=O)-N=N-NR^3 -, -C(=O)-NR^3-N=N-, -N=N-NR^3- -C(=N-$N(R^3)_2$)-, -C(=NR^3)-, -C(=O)O-, -C(=O)S- -C(=S)-, -O-P(=O)$_2$O-, -R^3O-, -R^3S-, -S-C=N-and -C(=O)-NR^3-O-, wherein groups with two chemically nonequivalent termini can adopt both possible orientations;

the $-(CH_2)_{pNPL}-$ alkylene chain is optionally substituted with one or more amino or hydroxy groups, or is unsaturated;

pNPL is 0 to 8;

q1NPL and q2NPL are independently 0, 1 or 2;

PL is a polar group selected from the group consisting of halo, hydroxyethoxymethyl, methoxyethoxymethyl, polyoxyethylene , and $-(NR^{5'})_{q1PL}-U^{PL}-(CH_2)_{pPL}-(NR^{5'})_{q2PL}-V$, wherein:

R^5, $R^{5'}$, and $R^{5''}$ are independently selected from the group consisting of hydrogen, alkyl, and alkoxy;

UPL is absent or selected from the group consisting of O, S, S(=O), $S(=O)_2$, NR^5, -C(=O)-, -C(=O)-N=N-NR^5-, -C(=O)-NR^5-N=N-, -N=N-NR^5-, -C(=N-N(R5)$_2$)-, -C(=NR5)-, -C(=O)O-, -C(=O)S- , -C(=S)-, -O-P(=O)$_2$O-, -R^5O, -R^5S-, -S-C=N-and -C(=O)-NR^5-O-, wherein groups with two chemically nonequivalent termini can adopt both possible orientations;

V is selected from the group consisting of nitro, cyano, amino, hydroxy, alkoxy, alkylthio, alkyl amino, dialkylamino, $-NH(CH_2)_pNH_2$ wherein p is 1 to 4, diazamino, amidino, guanidino, guanyl, semicarbazone, aryl, heterocycle and

heteroaryl, any of which is optionally substituted with one or more of amino, halo, cyano, nitro, hydroxy, $-NH(CH_2)_pNH_2$ wherein p is 1 to 4, $-N(CH_2CH_2NH_2)_2$, amidino, guanidino, guanyl, aminosulfonyl, aminoalkoxy, aminoalkythio, lower acylamino, or benzyloxycarbonyl;

the $-(CH_2)_{pPL}$-alkylene chain is optionally substituted with one or more amino or hydroxy groups, or is unsaturated;

pPL is 0 to 8;

q1PL and q2PL are independently 0, 1 or 2; and

m is 1 to about 20; and a pharmaceutically acceptable carrier or diluent.